OIPE JC141
AUG 23 2004
PATENT & TRADEMARK OFFICE

FIGURE 1

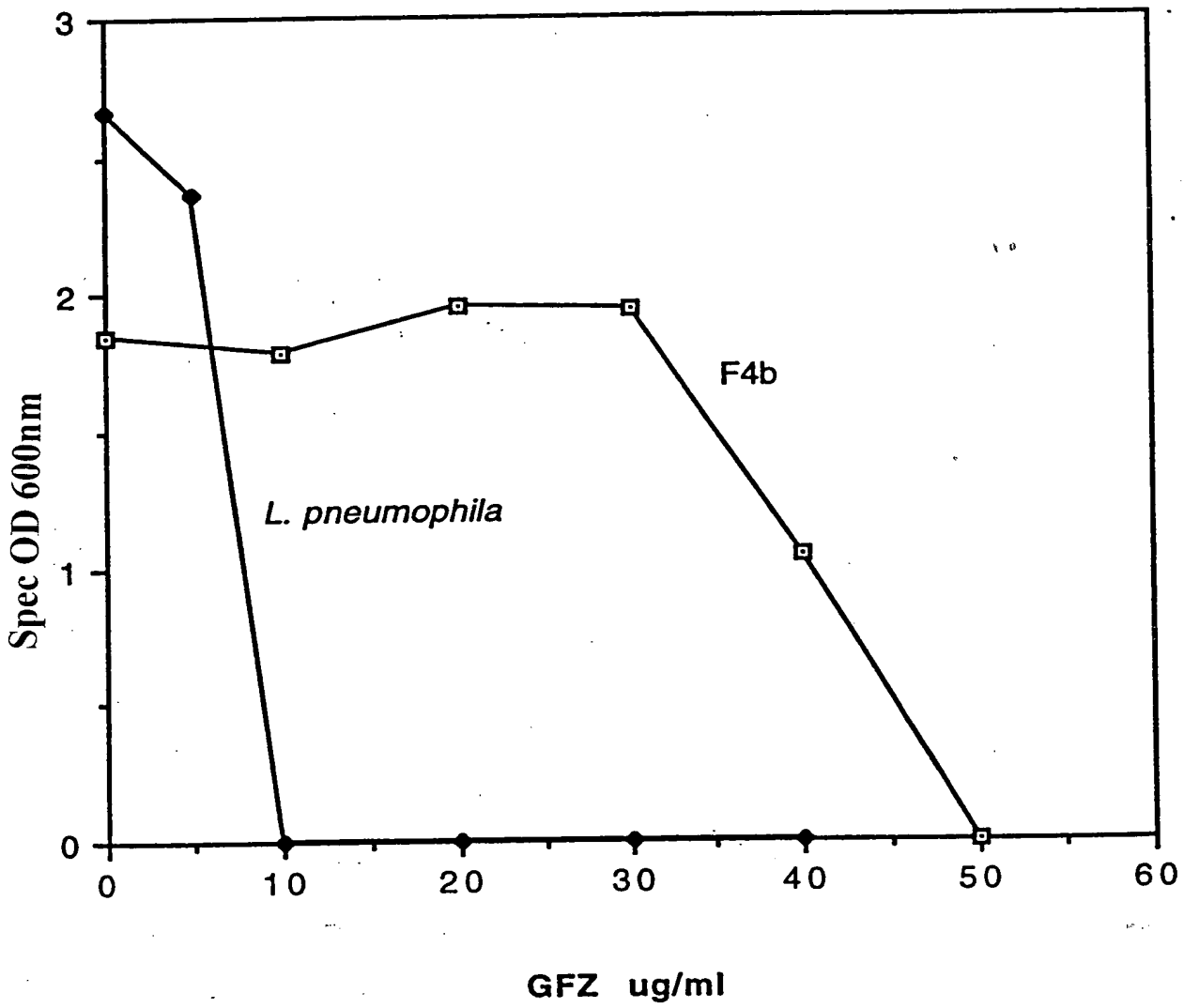

FIGURE 2

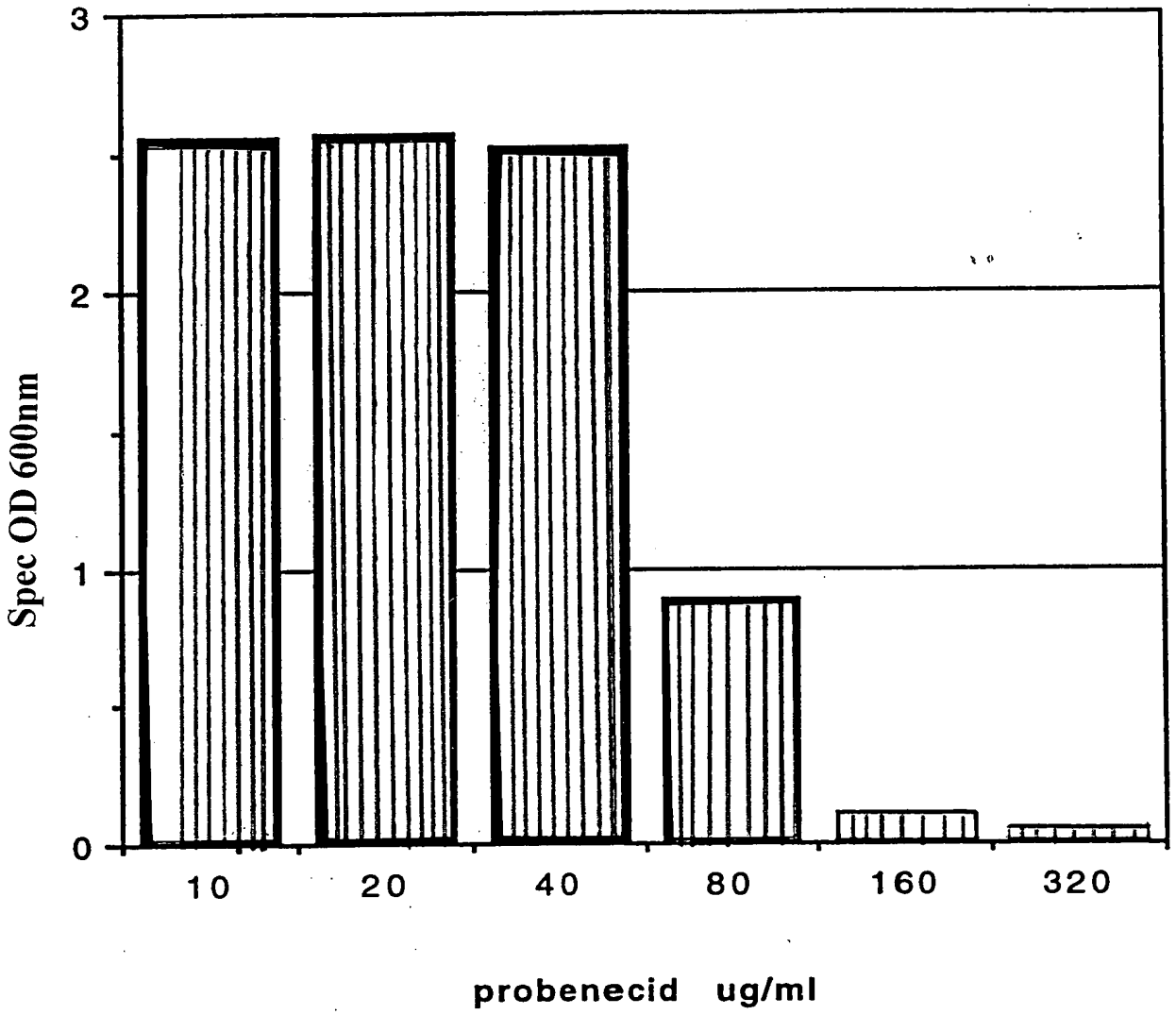

FIGURE 3

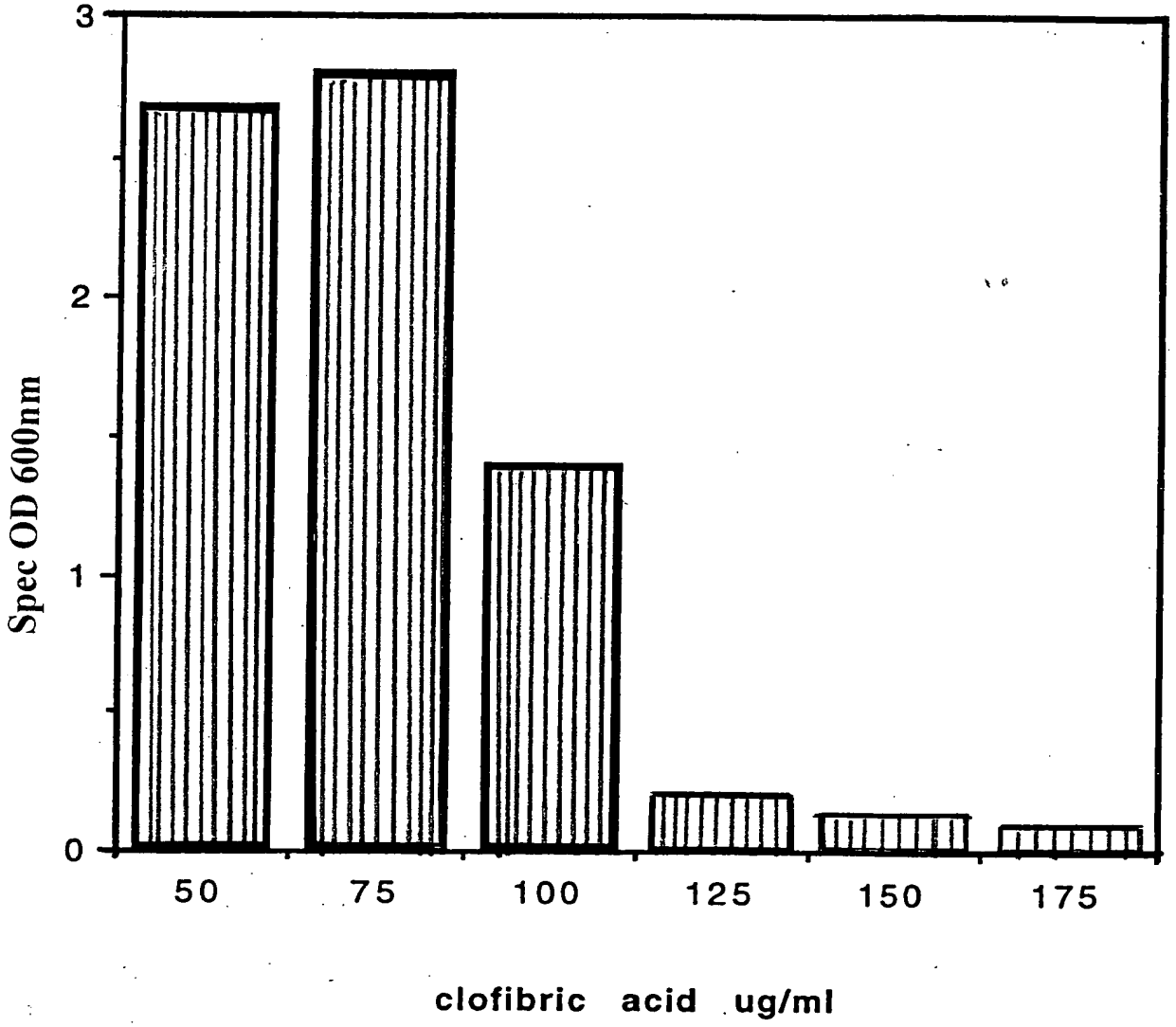

FIGURE 4

Sensitivity Screen

Organism	Sensitive?
Legionella pneumophila	**yes**
Acinetobacter sp.	no
Actinobacillus sp.	no
Azobacter vinlandi	no
Bacillus aureus	no
Bacillus subtilis	**yes**
Cardiobacterium sp.	no
Caulobacter crescentus	**yes**
Citrobacter freundi	yes
(4) Corynebacterium sp.	no
Enterobacter cloacae	no
Enterococcus faecalis	no
Escherichia coli	no
Klebsiella pneumonia	no
Leuconostoc sp.	no
(6) Nocardia sp.	**yes**
Pediococcus sp.	no
Proteus mirabilis	no
Pseudomonas aeruginosa	no
Rhizobium nulilo	no
Rhodobacter spheroides	**yes**
(3) Rhodococcus sp.	no
Salmonella sp.	no
Serratia marcescens	no
Shigella sp.	no
Xanthomonas sp.	no
(5/6) Group A Streptococcus sp	no
(1/6) Group A Streptococcus sp.	**yes**
(3) Coag neg Staphylococcus aureus	**yes**
(3) Coag pos Staphylococcus aureus	no
Mycobacterium tuberculosis	**yes**
Mycobacterium chelonei	no
Mycobacterium fortuitum	no

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FIGURE 6A

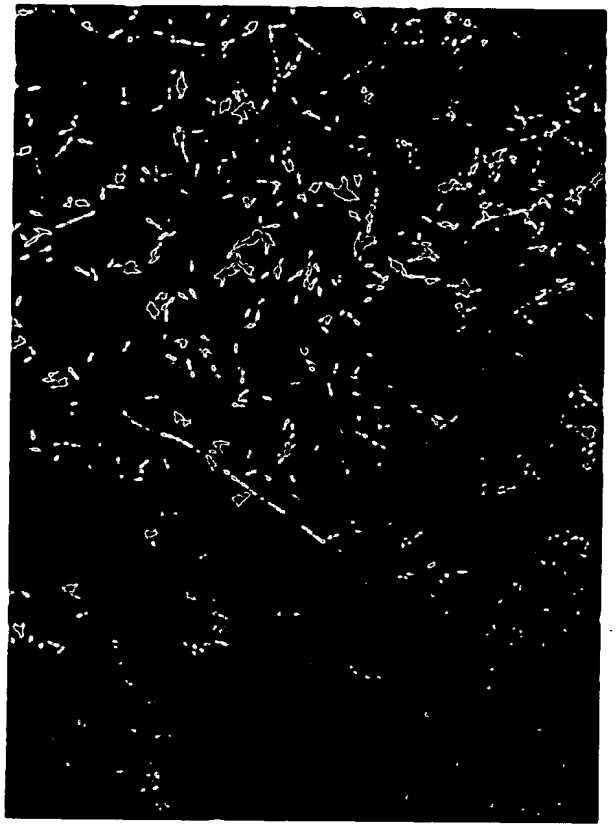

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FIGURE 6B

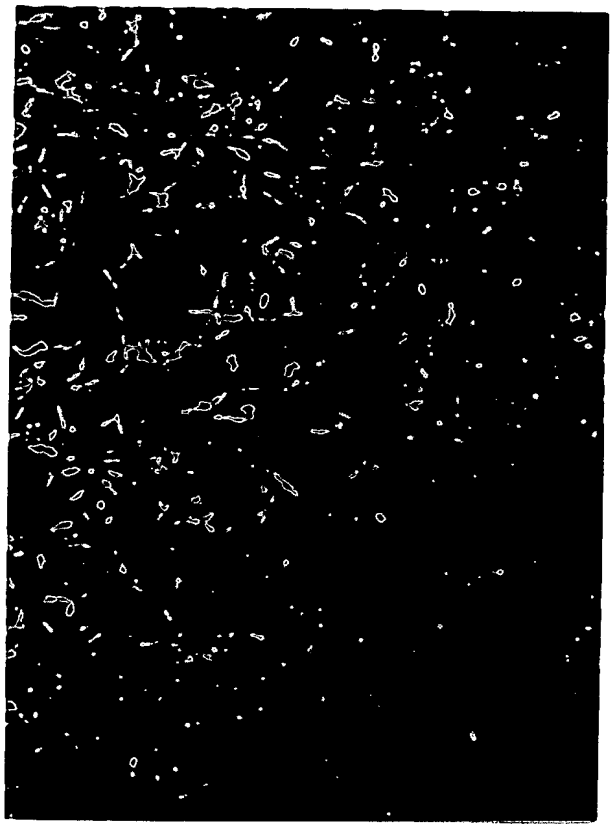

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FIGURE 7

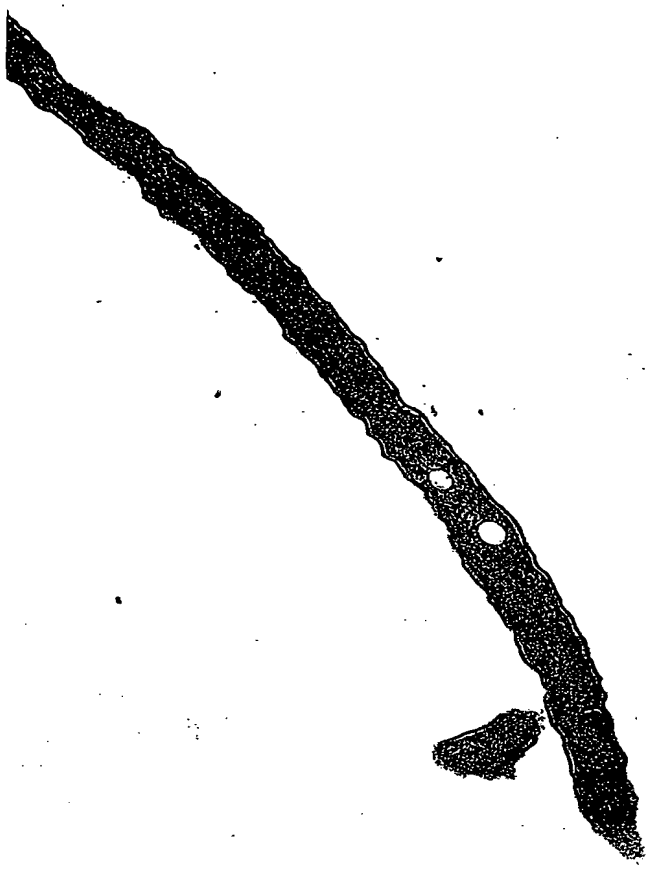


FIGURE 8

FIGURE 9B

F4b 4.5 (-GFZ)

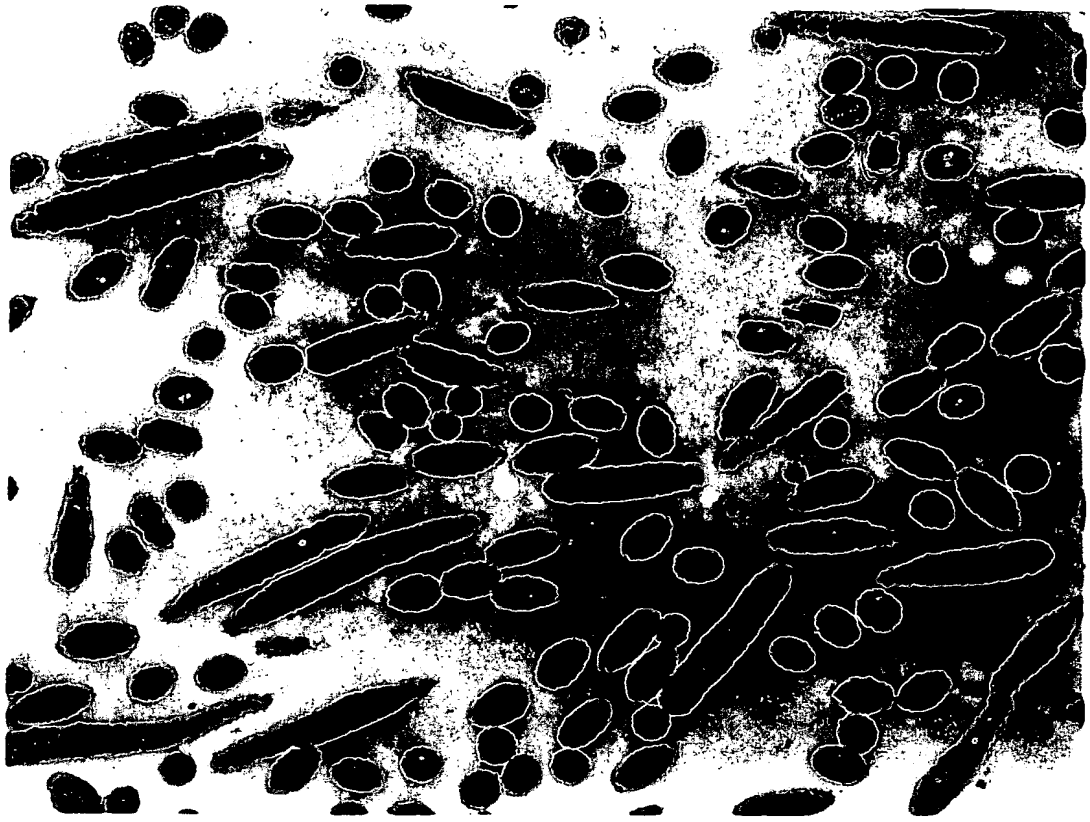


FIGURE 9A

L.pneumophilia 4.5 hrs (-GFZ)

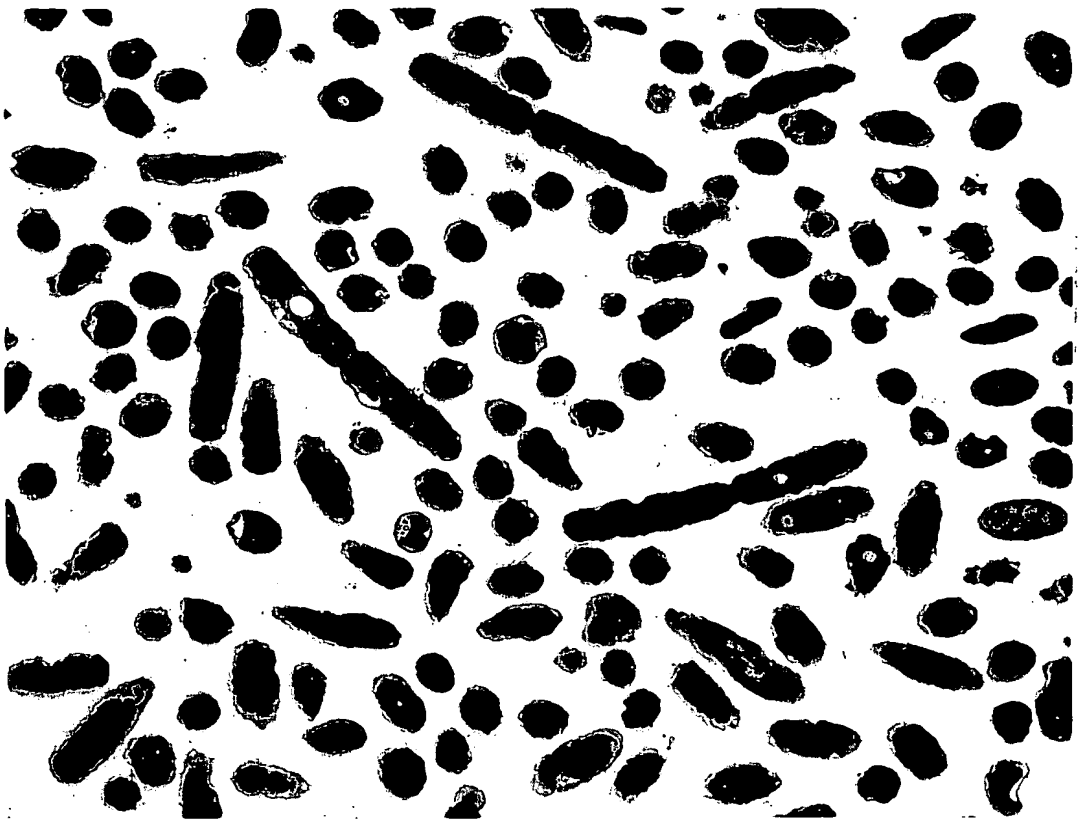


FIGURE 9D

F4b 4.5 (-GFZ)

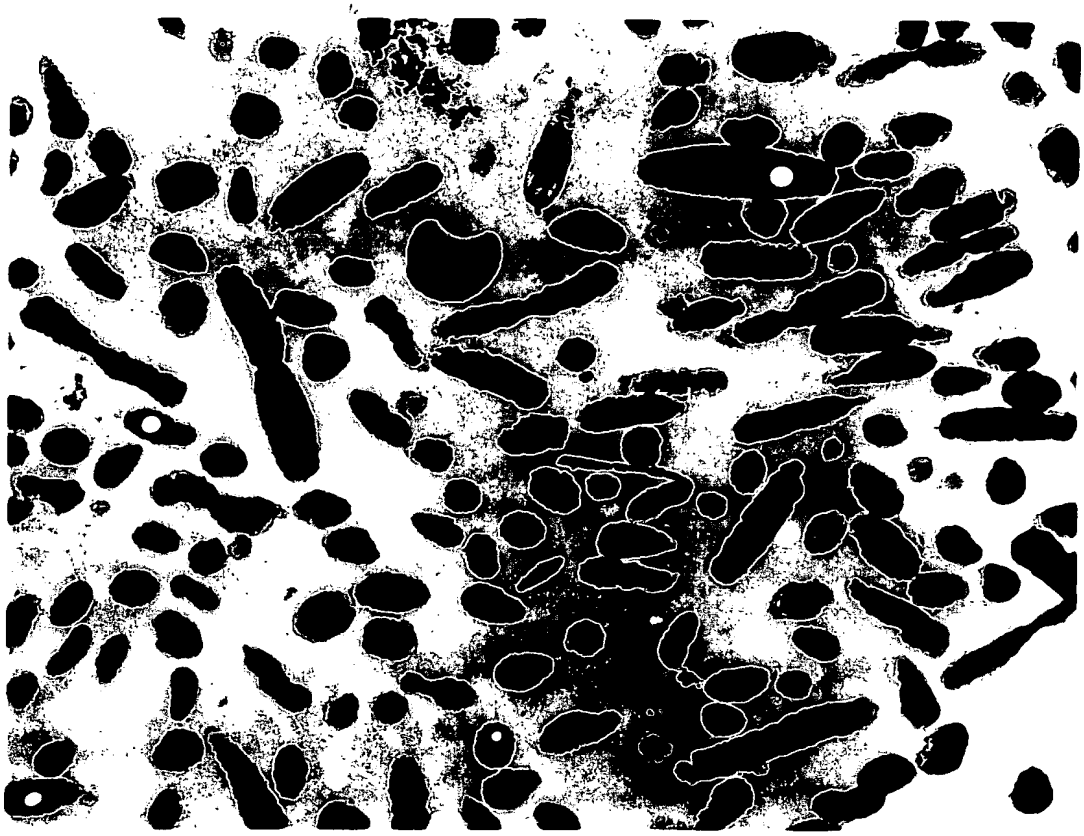


FIGURE 9C

L.pneumophilia 4.5 hrs (-GFZ)

FIGURE 5

MDR-*M. tuberculosis* Sensitivity to GFZ

Strain	GFZ 0ug/ml	GFZ 25ug/ml	GFZ 50ug/ml	GFZ 100ug/ml	GFZ 200ug/ml
W54410	++	+	35	-	-
5260	++	++	43	-	-
T30234	++	++	+	-	-
O81256	++	++	+	-	-
W19521	++	++	+	-	-
O80154	+++	++	+	-	-
CDC N	++	ND	+	-	-
H52578	++	++	++	-	-
CDC P	+++	ND	+++	-	-
O80711	++	++	+	6	-
S 15674	++	++	+	10	-
M23294	++	++	++	4.5	-
CDC K	+++	ND	++	6	-
M41151	++	++	++	7.5	-
F16285	++	++	++	10	-
T45777	+++	+++	+++	+	-
Avanto	+++	ND	+++	+	-
Harrison	+++	ND	+++	+	-
CDC L	+++	ND	++++	++	-
Montalvo	++++	ND	++++	++	-
MTB2517	++++	ND	++++	++	-

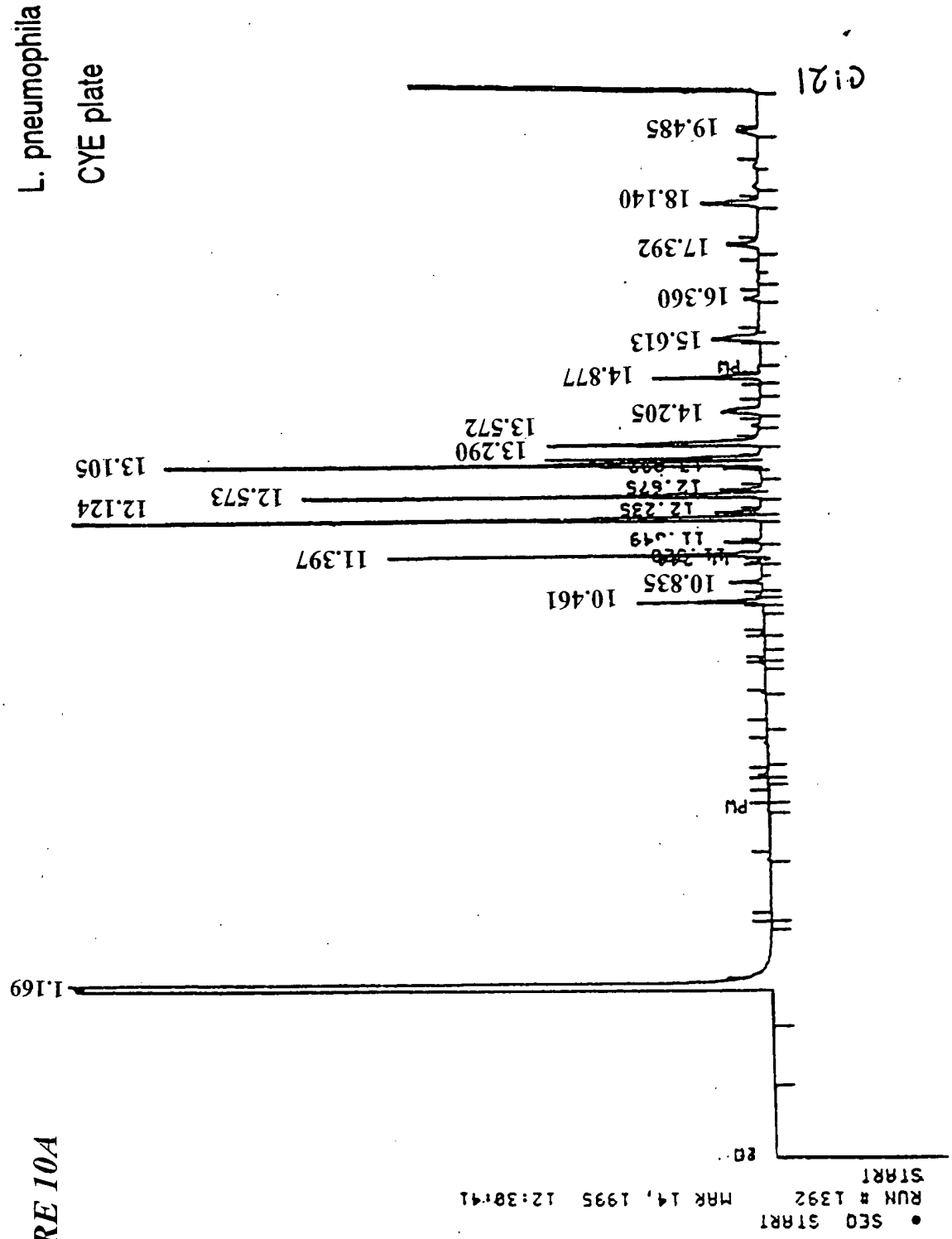

L. pneumophila
CYE plate
19.485
18.140
17.392
16.360
15.613
14.877
14.205
13.572
13.290
13.105
12.573
12.124
11.397
10.835
10.461
1.169
PU
ED
• SEQ START
RUN # 1392 MAR 14, 1995 12:38:41
START

FIGURE 10A

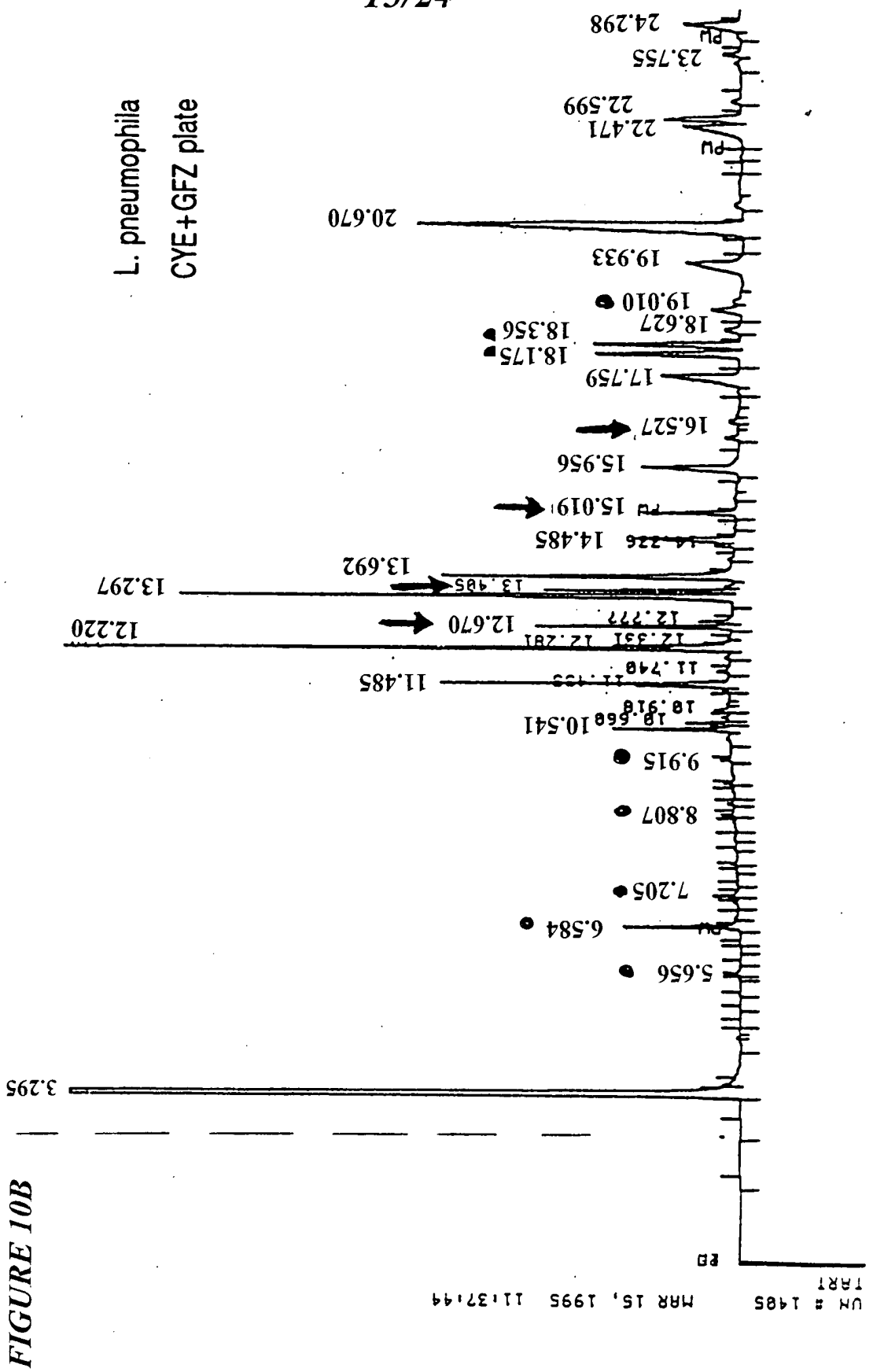

L. pneumophila
CYE+GFZ plate
3.295
5.656
6.584
7.205
8.807
9.915
10.541
11.485
12.220
12.670
13.297
13.692
14.485
15.019
15.956
16.527
17.759
18.175
18.356
18.627
19.010
19.933
20.670
22.471
22.599
23.755
24.298

FIGURE 10B

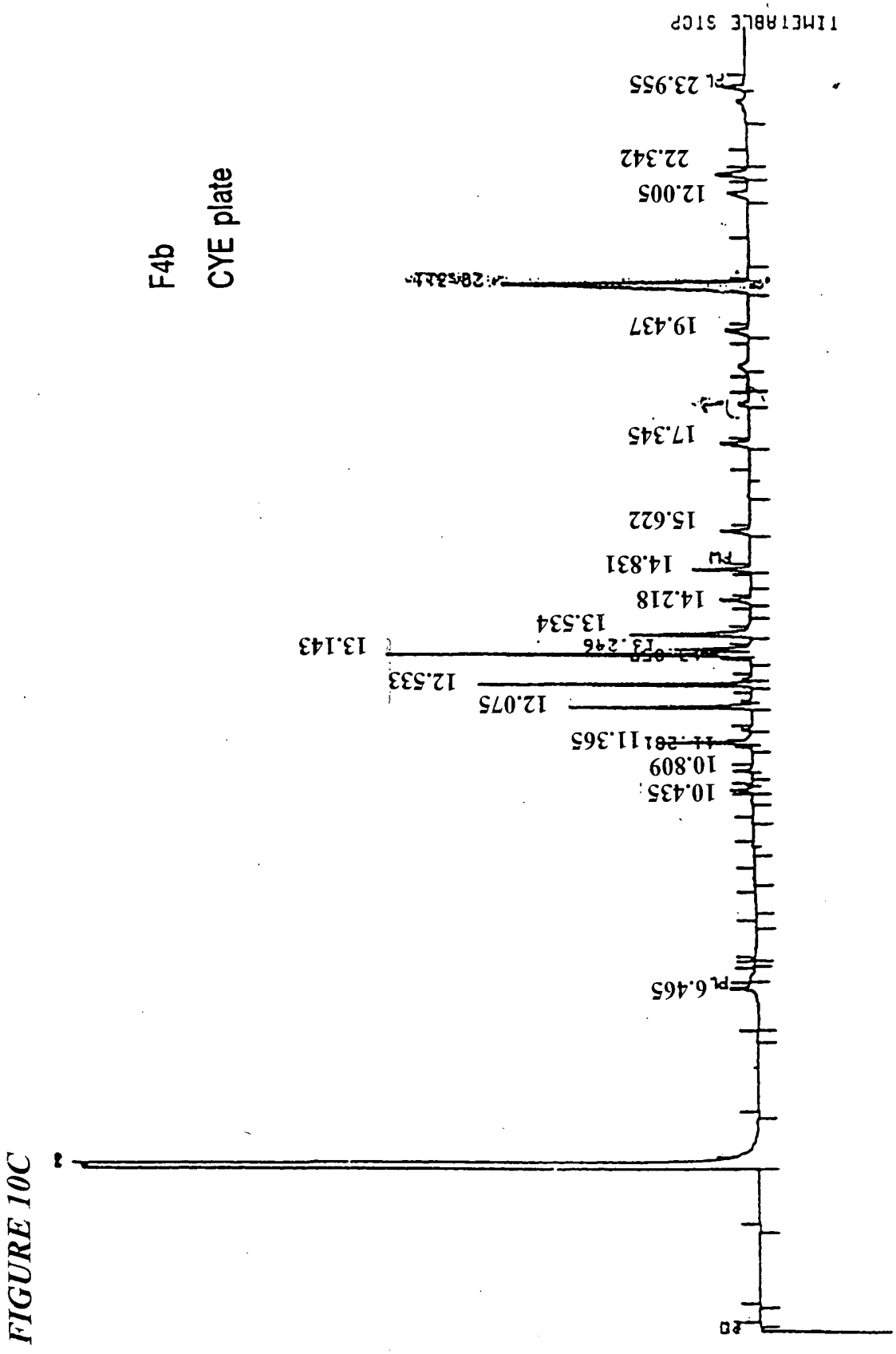

F4b
CYE plate
TIME TABLE STCP
23.955
22.342
12.005
19.437
17.345
15.622
14.831
14.218
13.534
13.143
12.533
12.075
11.365
10.809
10.435
6.465

FIGURE 10C

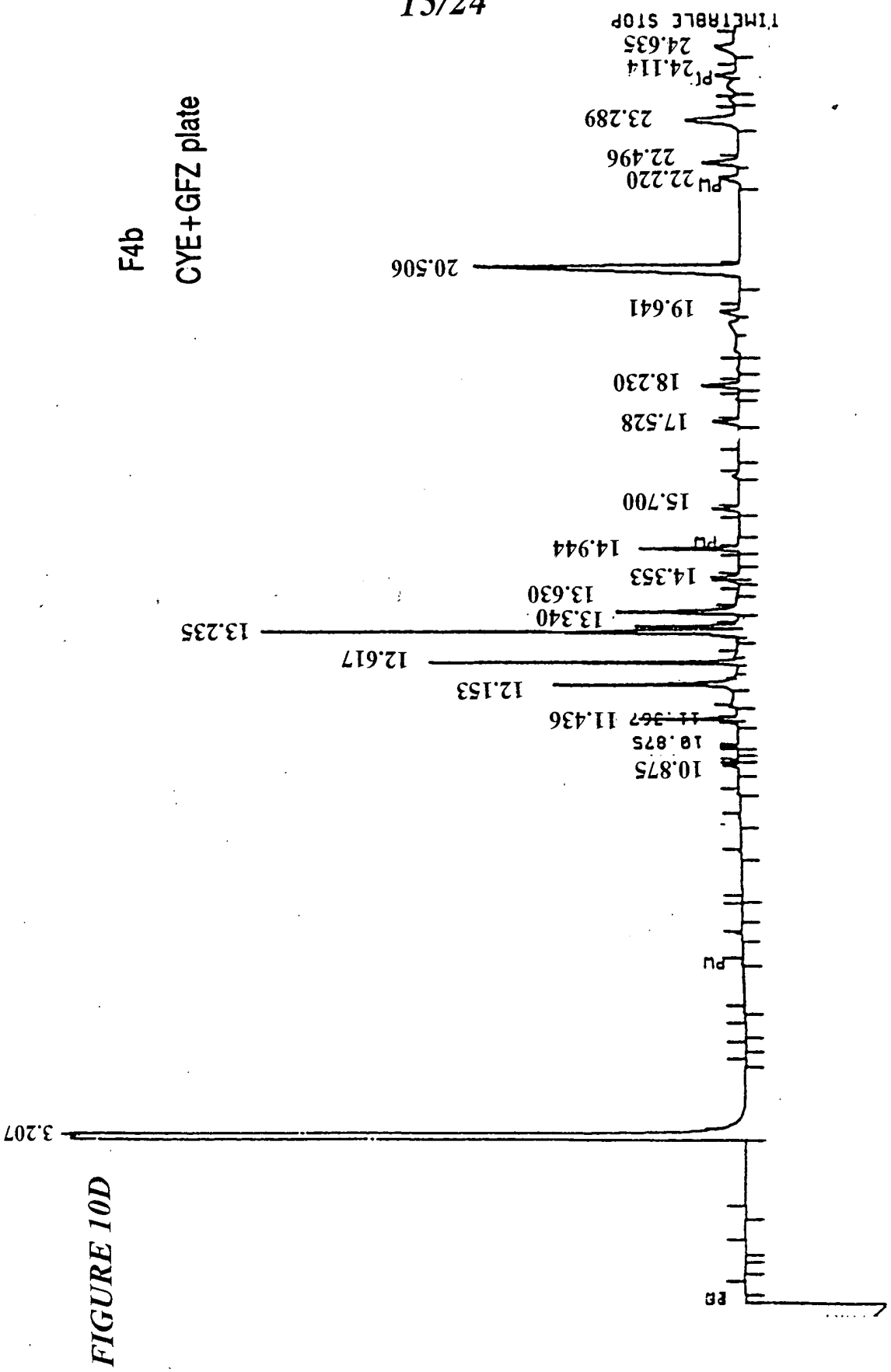
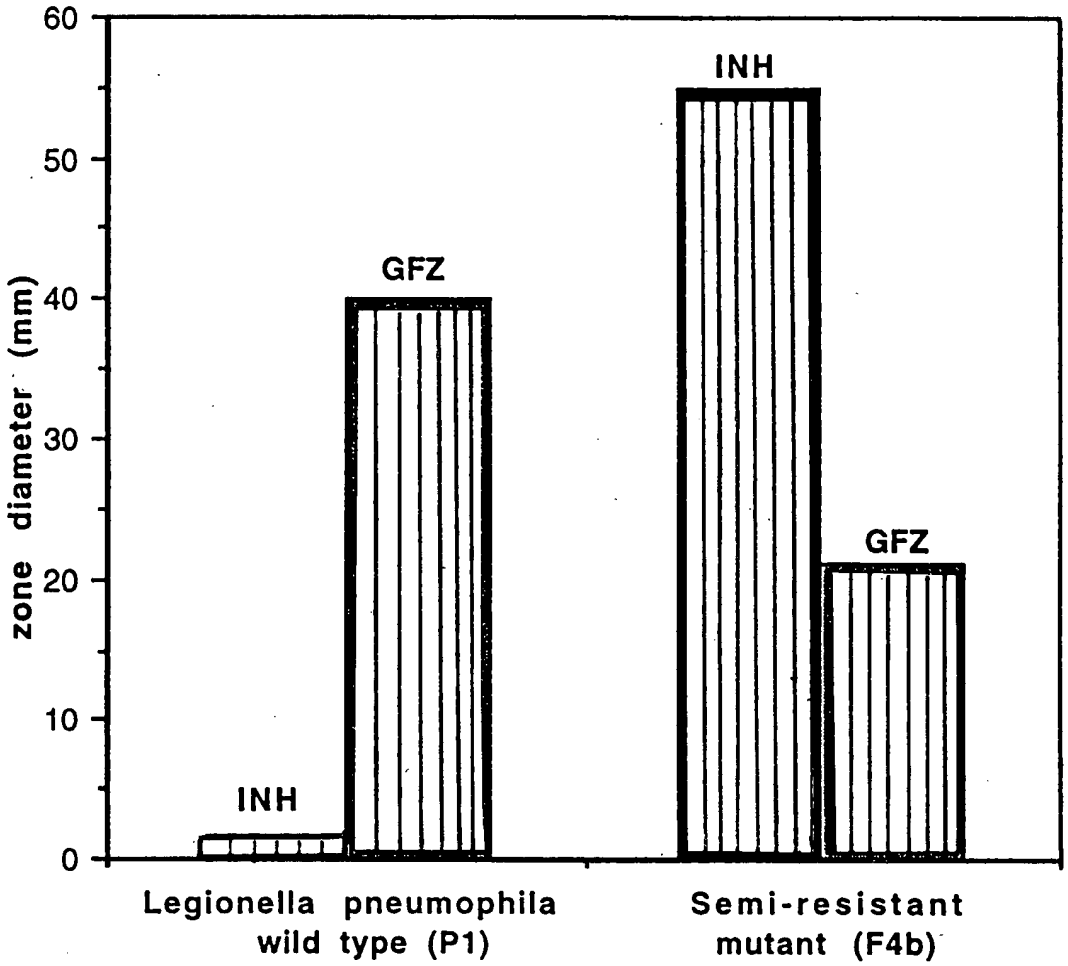

F4b
CYE+GFZ plate
TIMETABLE STOP
24.635
PU 24.114
23.289
PU 22.220
22.496
20.506
19.641
18.230
17.528
15.700
PU 14.944
14.353
13.630
13.340
13.235
12.617
12.153
11.436
10.875
10.875
PU
3.207
PB

FIGURE 10D

FIGURE 11


60
50
40
30
20
10
0
zone diameter (mm)
INH
GFZ
INH
GFZ
Legionella pneumophila
wild type (P1)
Semi-resistant
mutant (F4b)

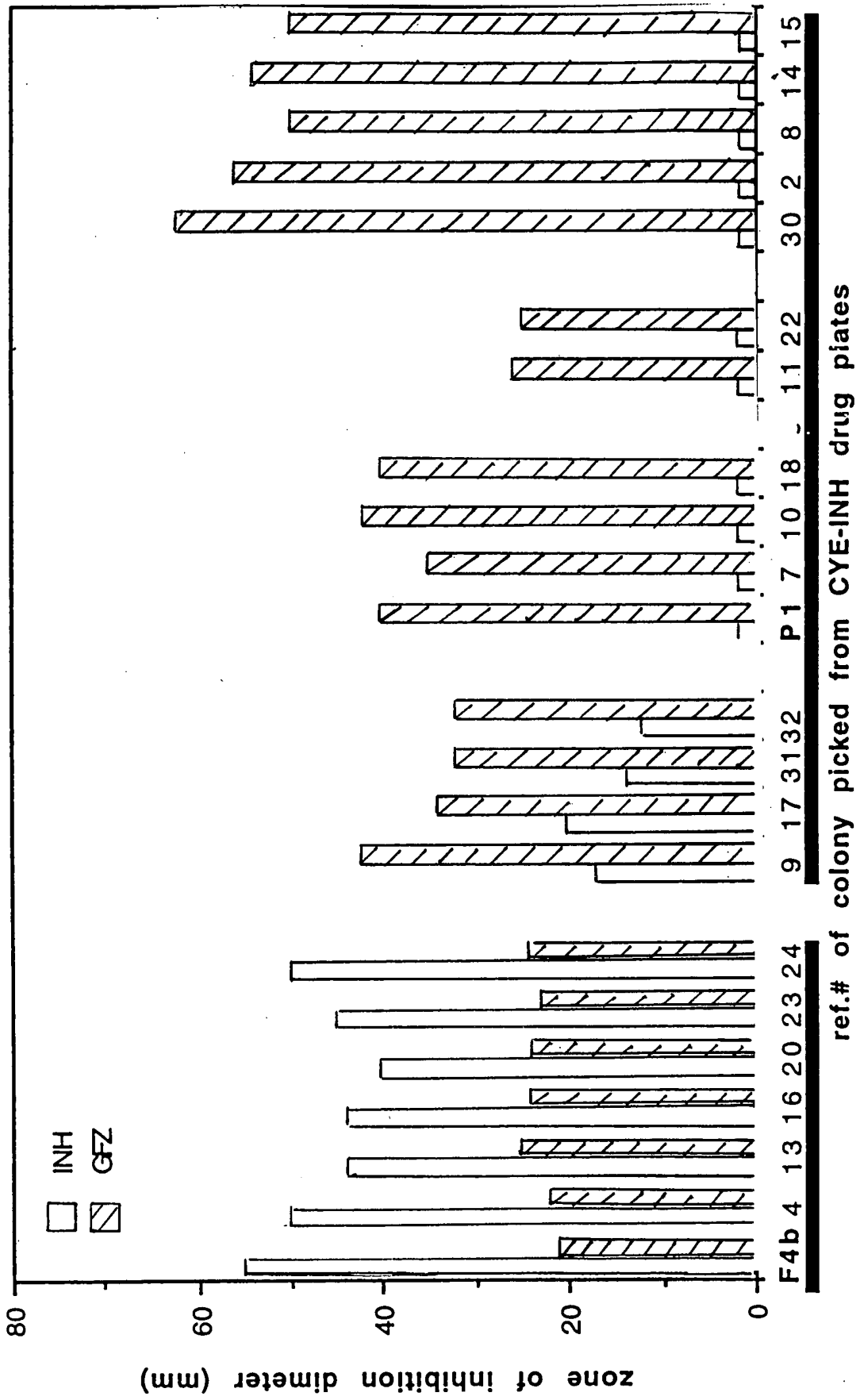
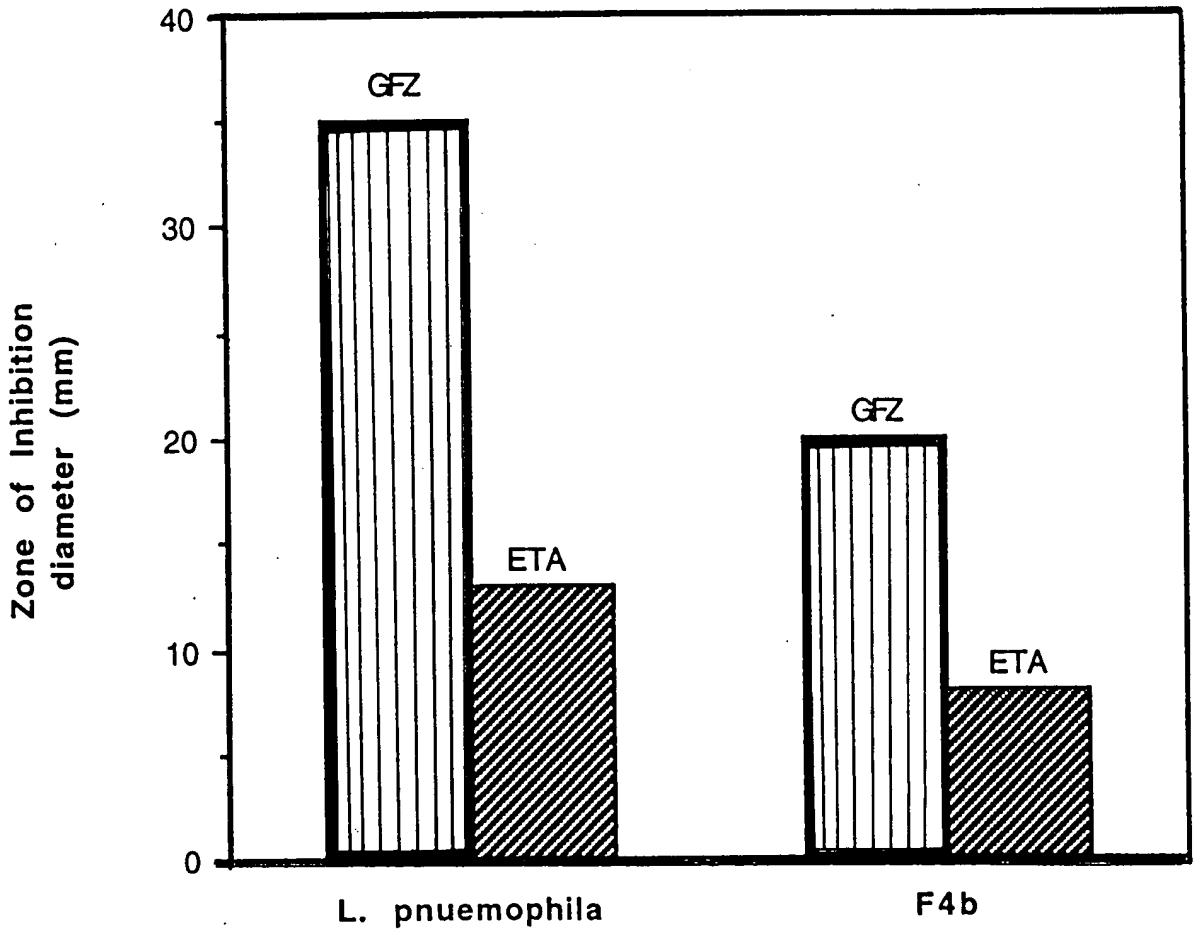

zone of inhibition diameter (mm)
0
20
40
60
80
INH
GFZ
F4b 4 13 16 20 23 24
9 17 31 32
P1 7 10 18
11 22
30 2 8 14 15
ref.# of colony picked from CYE-INH drug plates

FIGURE 12

FIGURE 13


40
30
20
10
0
Zone of Inhibition diameter (mm)
GFZ
ETA
GFZ
ETA
L. pnuemophila
F4b

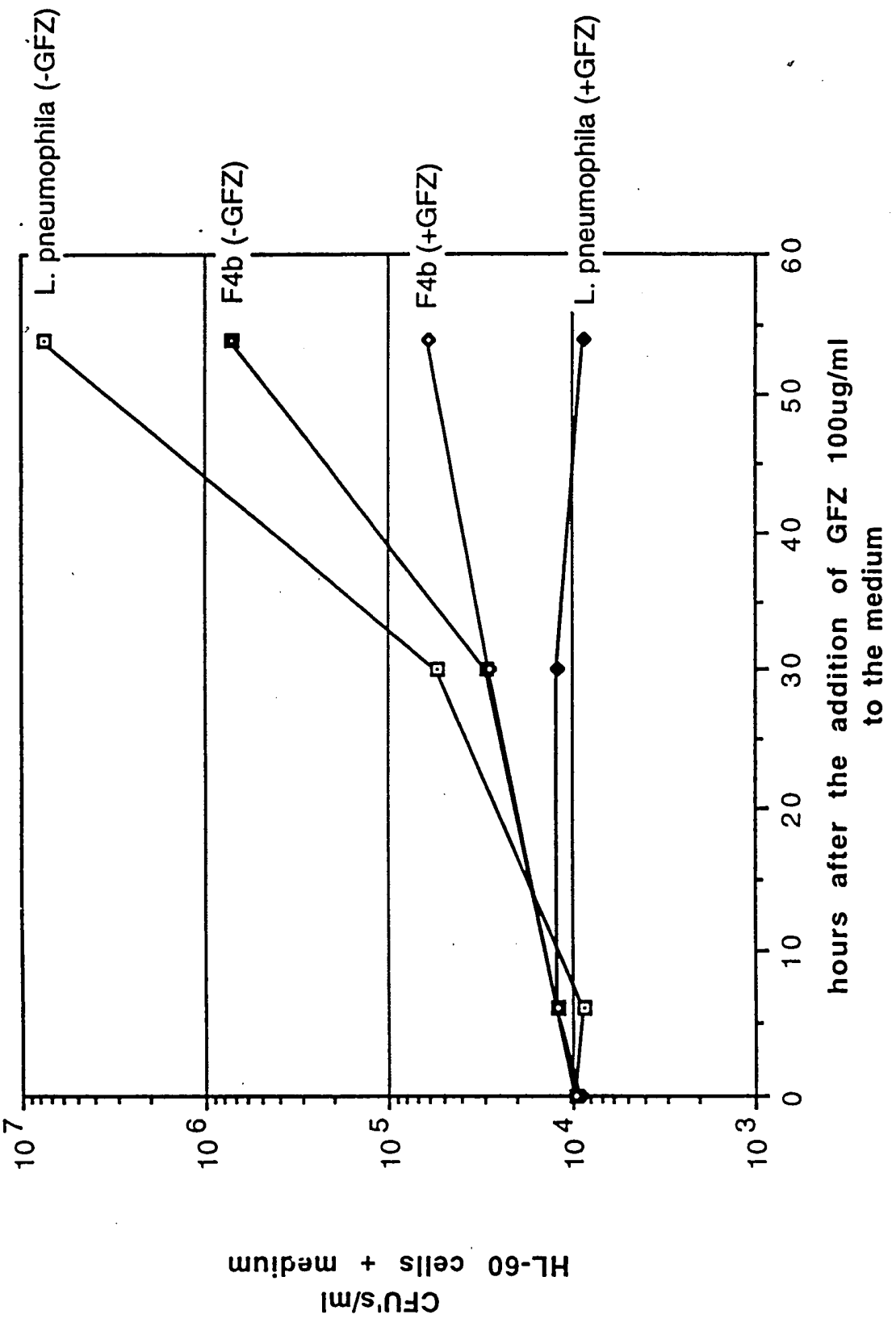
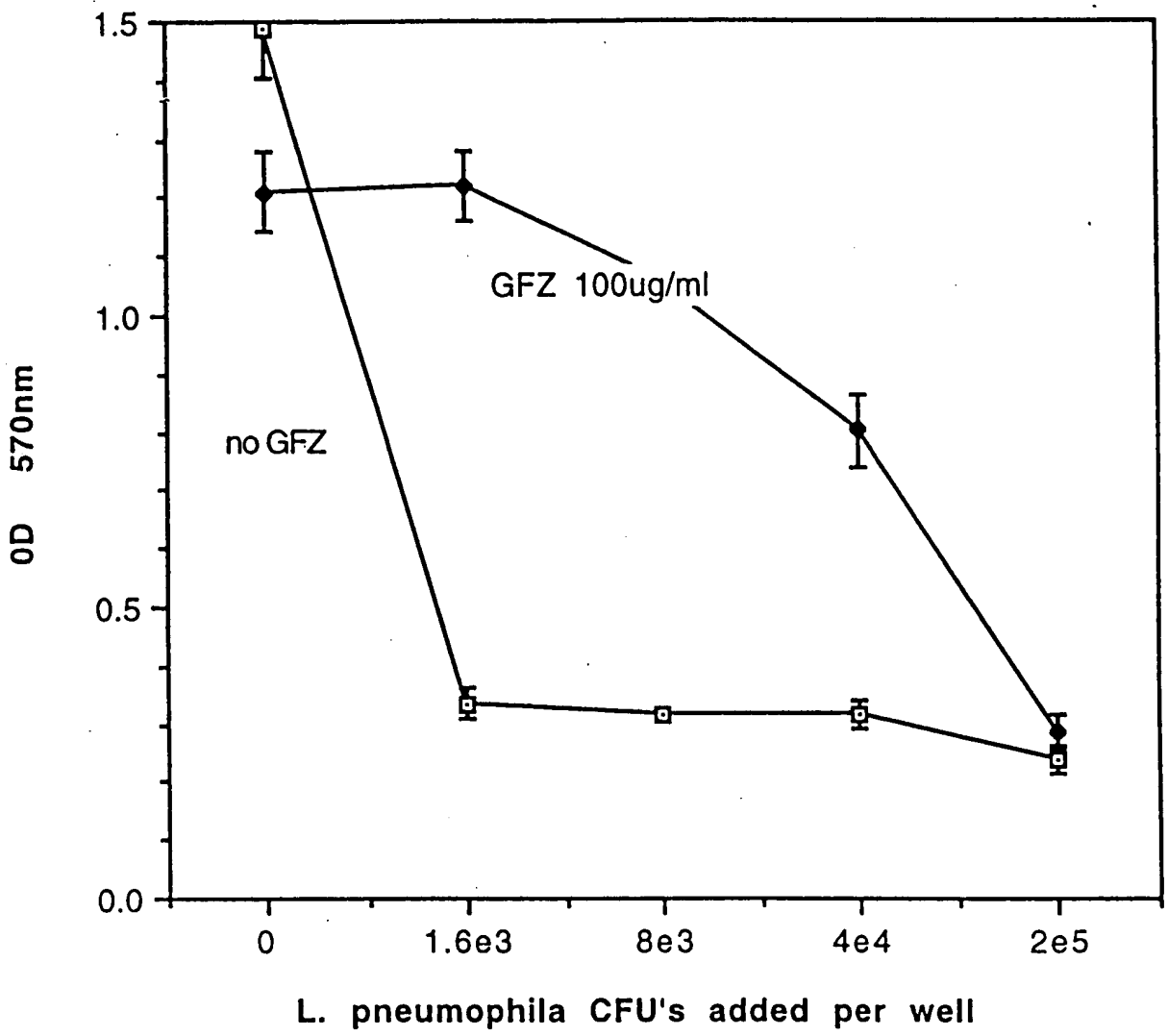

L. pneumophila (-GFZ)
F4b (-GFZ)
F4b (+GFZ)
L. pneumophila (+GFZ)
CFU's/ml
HL-60 cells + medium
10^7
10^6
10^5
10^4
10^3
0
10
20
30
40
50
60
hours after the addition of GFZ 100ug/ml
to the medium

FIGURE 14A

FIGURE 14B


1.5
1.0
0.5
0.0
OD 570nm
GFZ 100ug/ml
no GFZ
0
1.6e3
8e3
4e4
2e5
L. pneumophila CFU's added per well

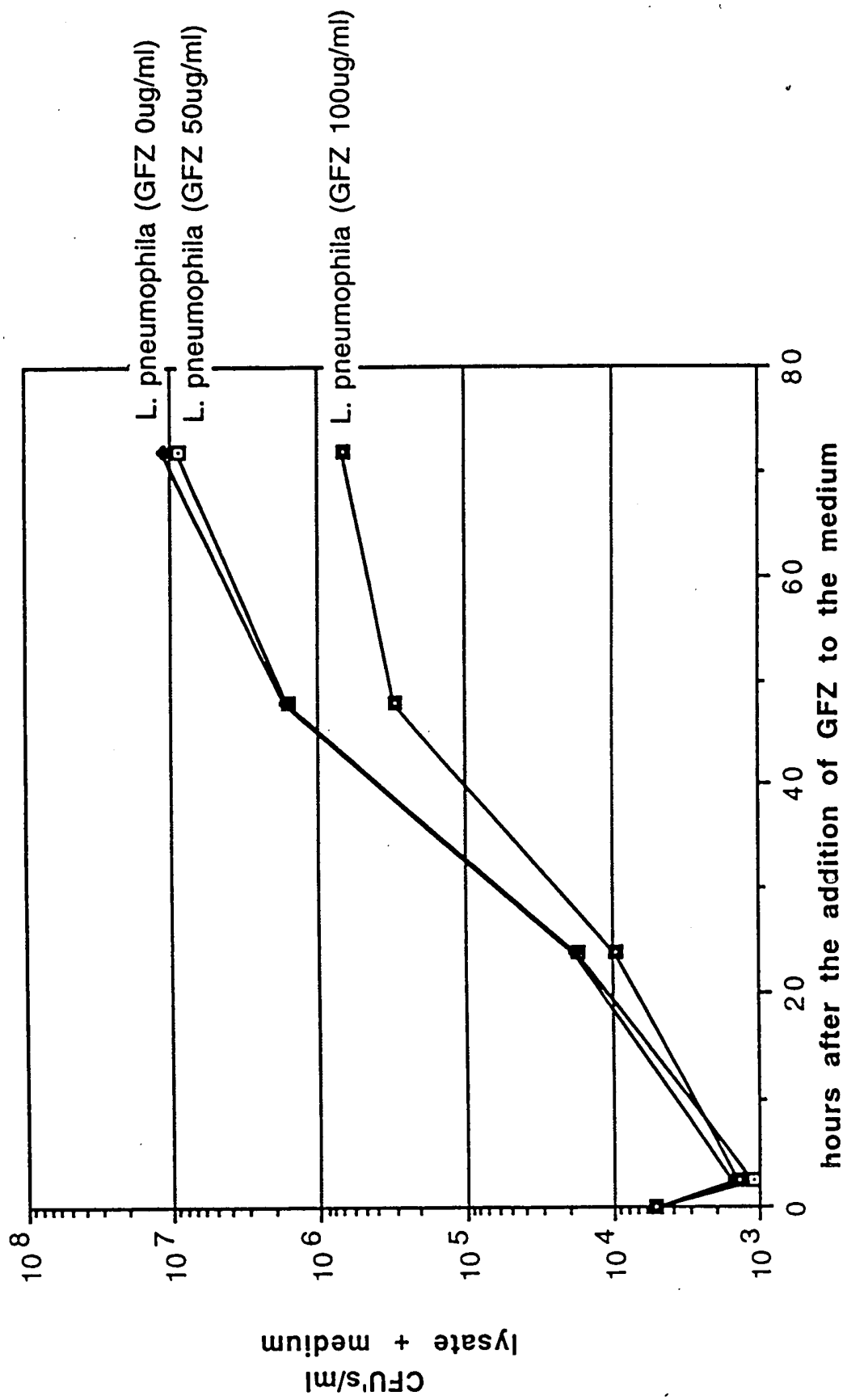

L. pneumophila (GFZ 0ug/ml)
L. pneumophila (GFZ 50ug/ml)
L. pneumophila (GFZ 100ug/ml)
CFU's/ml
lysate + medium
10^8
10^7
10^6
10^5
10^4
10^3
0
20
40
60
80
hours after the addition of GFZ to the medium

FIGURE 15A

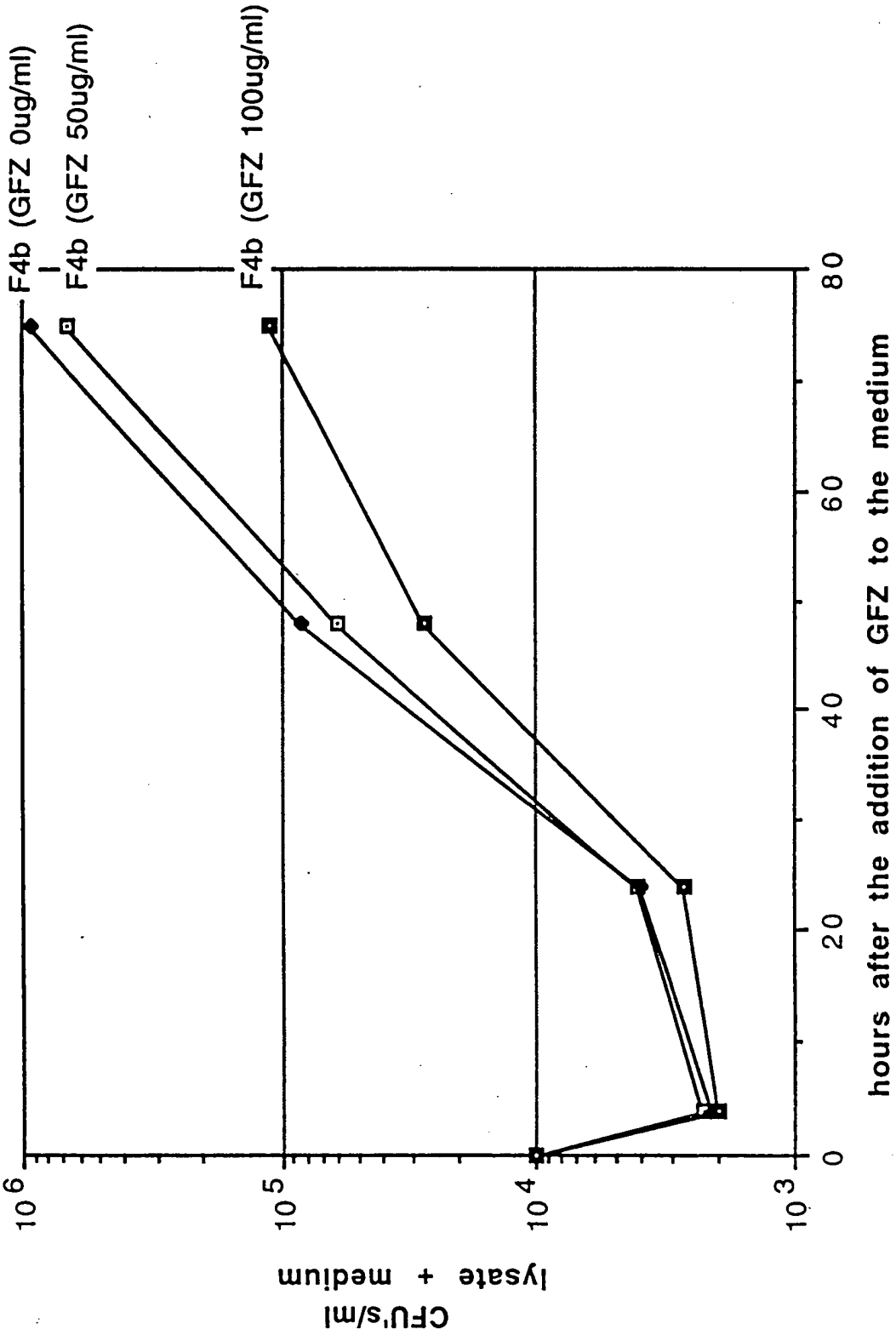

F4b (GFZ 0ug/ml)
F4b (GFZ 50ug/ml)
F4b (GFZ 100ug/ml)
CFU's/ml
lysate + medium
10^6
10^5
10^4
10^3
0
20
40
60
80
hours after the addition of GFZ to the medium

FIGURE 15B

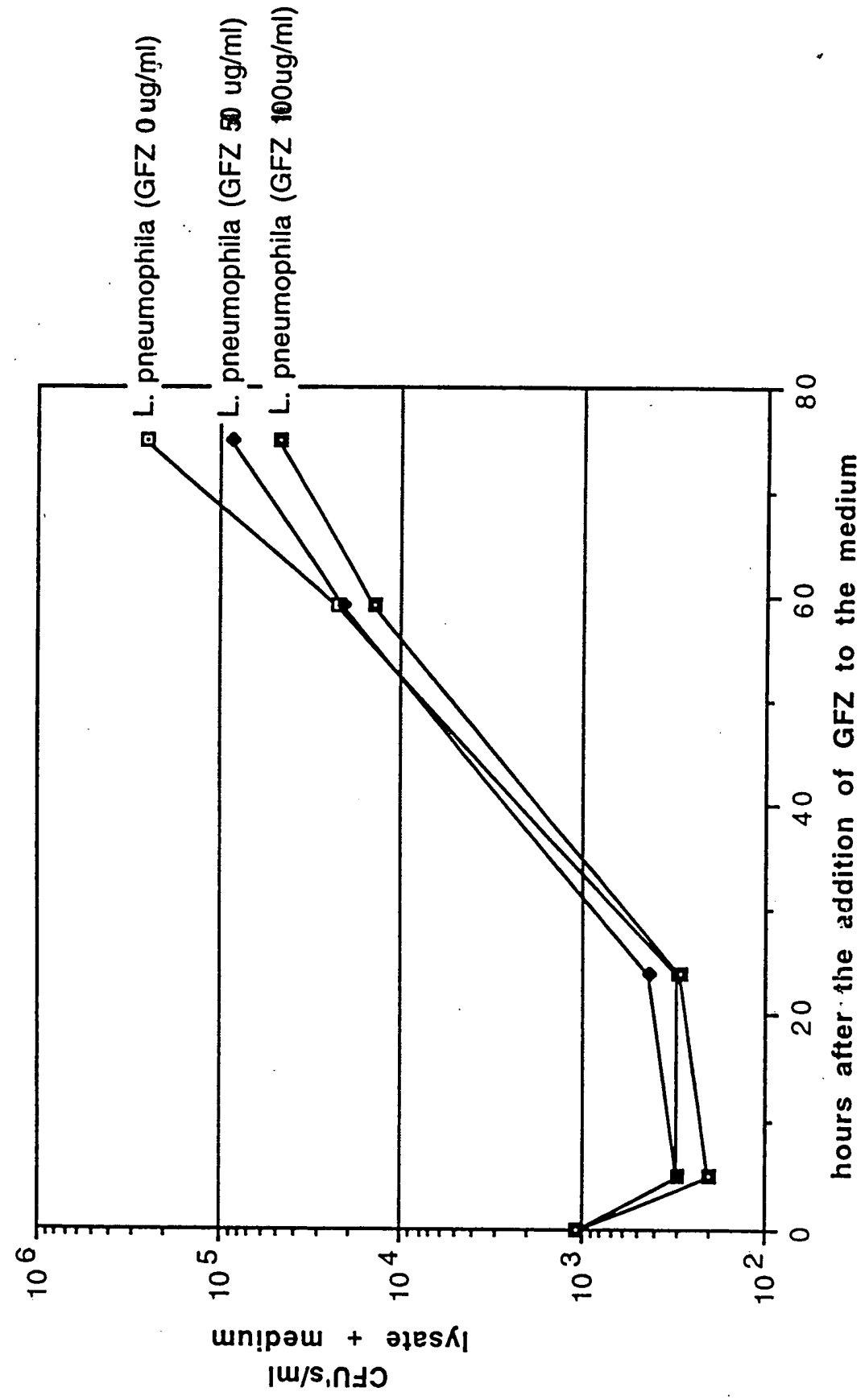

L. pneumophila (GFZ 0 ug/ml)
L. pneumophila (GFZ 50 ug/ml)
L. pneumophila (GFZ 100ug/ml)
CFU's/ml
lysate + medium
10^6
10^5
10^4
10^3
10^2
0
20
40
60
80
hours after the addition of GFZ to the medium

FIGURE 15C

FIGURE 16

	Zones of Inhibition diameter (mm)	
	Permissive Temperature	Restrictive Temperature
STRAIN	30C	42C
ts100	0	no growth
ts100:pBSK	0	no growth
ts100:pBSK2.1	0	19
101envM+	0	0
101envM+:pBSK	0	0
101envM+:pBSK2.1	0	0
DH5a	0	0
DH5a:pBSK	0	0
DH5a:pBSK	0	0